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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/431,607	11/01/1999	LOUIS E. HENDERSON	15280-169300	8955

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EXAMINER

FOLEY, SHANON A

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 07/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/431,607

Applicant(s)

HENDERSON ET AL.

Examiner

Shanon Foley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 11 April 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 24-29 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 24-29 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

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## DETAILED ACTION

### *Priority*

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). Application 08/379,420 and its current status is not listed on the first line of the specification.

This requirement is repeated because applicant has not responded to the priority requirements.

### *Claim Objections*

It is noted that original claims 22 and 23 were not cancelled along with original claims 1-21 in pre-amendment A of paper no. 4. In that paper, applicant added claims 22-27. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 22-27 been renumbered 24-29.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 24-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

Applicant asserts that the claims are definite because "NO derivatives" refer to nitric oxide and any molecule containing a nitric oxide group, which would be readily recognizable by one skilled in the art as suitable electron acceptors. Applicant further points to passages in the specification to support "NO derivatives" that are able to accept zinc electrons from the CCHC finger.

Applicant's assertions as well as a review of the excerpts cited in the instant disclosure have been reviewed, but are found to be unpersuasive. The metes and bounds for determining what a "derivative" of an NO group is cannot be discerned because of the exclusionary language in the claim drawn to molecules containing an "NO" group, i.e., R-C-NO. This molecule has a nitric oxide group and, according to applicant's arguments, would be considered an electron acceptor in the art. Since this group of molecules containing the "NO" group are specifically excluded and are obviously "derivatives containing the NO group" in line 7 of claim 24, it cannot be determined what other molecules comprising an "NO" group are also intended to be excluded. Also, because the NO derivative, R-C-NO, is an NO derivative and is expressly excluded from the claims, it cannot be determined what an "NO derivative" is, structurally or functionally. If NO derivatives are structural derivatives, then the "NO derivatives" would not necessarily contain an NO group, and if the NO derivatives are functional derivatives, the "NO derivatives" would not be required to perform a parallel function of an NO group. Considering the all of the dimensions of ambiguity encompasses by the phrase, "derivatives containing the

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NO group” and the exclusionary proviso of the NO derivative, R-C-NO in line 7 of the claim, it is maintained that the claims are vague and indefinite.

Regarding the rejection against cupric or ferric ion complexes, applicant asserts that complexes comprising these ions are readily recognizable in the art as electron acceptors and points to literal support in the specification for cupric chloride and ferric acetate.

Applicant’s arguments as well as a review of the citations in the disclosure have been considered, but are found to be unpersuasive. It is unclear why applicant cited page 3, lines 21-24 in the rebuttal since the passage does not discuss cupric or ferric ions, or clarify what is considered a “complex” of either. Although it is conceded that the skilled artisan would readily recognize a ferric ion or a cupric ion, it is maintained that there is ambiguity for what a “complex” of either ion would be.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection maintained for reasons of record.

Applicant argues that it is known in the art at the time of the invention that R-C-NO inactivates retroviruses as taught by Rice et al., cited by the Office, but it was not known that the compounds dissociate zinc from CCHC zinc fingers. Applicant states that the negative limitation

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excluding the R-C-NO compounds is added to the claims to explicitly exclude using these compounds.

Applicant appears to be arguing the lack of anticipation of the cited reference and does not appear to refute the new matter rejection. Applicant has not indicated where support for this negative limitation can be found explicitly or implicitly in the disclosure. Therefore, it is maintained that there is no support in the specification for excluding R-C-NO compounds, especially in view of the claims encompassing the use of nitric oxide derivatives.

Claims 24-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection maintained for reasons of record.

Applicant summarizes the invention, which is drawn to disassociating zinc ions from CCHC retrovirus nucleocapsid zinc fingers with several classes of compounds. Applicant points to Figure 3 for support of retrovirus inactivation using a nitroso reagent, NOBA. Applicant also cites page 3, lines 18-24, and literal support for tetraethylthiuram disulfide on page 22, lines 25-26, cupric chloride on page 24, lines 6-12, and all of the compounds listed in Table 2 on pages 31-33 and pages 11-17. Applicant also cites the declaration of Dr. Rice and the exhibits provided with the response to the Office action that demonstrate that retrovirus nucleoproteins are structurally conserved and bind to zinc. Applicant asserts that in light of the references and the declaration of Dr. Rice, the skilled artisan would know that the instantly claimed compounds inactivate any retrovirus with a CCHC in their nucleocapsid proteins.

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Applicant indicates on page 6 referencing a footnote at the bottom of page 7 of the response, that a copy of the declaration by Dr. Rice and the exhibits submitted therewith in 08/379,420 is attached for the examiner's convenience in the current reply to the outstanding Office action. However, the declaration and the exhibits applicant discusses are not of record in the instant case. No copies of either have been found in the instant case and therefore, have not been officially considered. However, to expedite prosecution, the declaration and the exhibits referred to by applicant were found in the parent application, 08/379,420. In this rejection, the Office addresses the declaration and exhibits and would be considered official statements if applicant had submitted the papers for the record. Statements regarding the declaration presented in this Office action will be considered official if applicant submits the declaration of record.

Applicant's citations, the declaration of Dr. Rice, and the exhibits submitted have been considered, but are unpersuasive for demonstrating written description for possessing every complex containing a cupric ion or a ferric ion or derivatives of NO. The declaration and the exhibits submitted clearly demonstrate that retrovirus nucleocapsid proteins are structurally and functionally conserved. It is also been established by the declaration and the exhibits that retroviruses containing CCHC zinc fingers in the nucleocapsid proteins are inactivated by the instant compounds. (It should be noted that this has only been established for compounds that have been clearly defined.) The literal support for the specific compounds cited by applicant is also acknowledged. However, whether retrovirus CCHC zinc fingers are conserved and inactivated by the instant classes of compounds were never issues in the instant written description rejection. This rejection is drawn to a lack of written description for every compound

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that merely contains cupric or ferric ions and every possible NO derivative. Applicant has not demonstrated support for every possible NO derivative or how the skilled artisan would be able to structurally identify such derivatives. As discussed above, it cannot be discerned what is intended by an NO derivative because of the express exclusion of R-C-NO. The compounds have no defined structure, the specification does not reasonably convey possession of these undefined compounds, and the skilled artisan would not be able to structurally identify the compounds with the required function. Applicant does not convey possession of every ferric or cupric ion complex or NO derivative that may exist and has not demonstrated written description that identifies a range of structures containing cupric ions or ferric ions or NO derivatives that would immediately identify itself to one of skill in the art to practice the invention.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 24-26, 28, and 29 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Ryser et al. (PNAS. May 1994. 91: 4559-4563) for reasons of record.

Applicant argues that Ryser et al. teaches the reduction of HIV infection by inhibiting HIV thiol-disulfide interaction with receptors with certain agents and does not teach a composition comprising an inactivated retrovirus.



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Applicant's arguments and a review of the reference have been considered, but are found to be unpersuasive. Ryser et al. teaches reducing critical disulfides in the HIV envelope glycoprotein to inhibit viral entry. This reduction is a form of virus inactivation since the virus has reduced ability to enter and infect cells. Therefore, the cells comprising the inhibitory agents and disabled HIV anticipate a composition comprising an inactivated retrovirus.

Claims 24-29 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Williams et al. (WO 94/193321) for reasons of record.

Applicant argues that Williams et al. teaches compounds that inhibit HIV reverse transcriptase and does not teach a composition comprising an inactivated retrovirus that has been inactivated by contact with one of the instant compounds.

Applicant's arguments and a review of the reference have been considered, but are found to be unpersuasive because Williams et al. anticipates contacting HIV with the 12<sup>th</sup> disulfide reagent listed in Table 2 on page 31 of the instant disclosure, i.e., aldrithiol-2, CAS registry number 2127-03-9, which is clearly within the scope of the compounds of claim 24. Therefore, since inhibition of HIV reverse transcriptase is a form of viral inactivation, the cell culture comprising 2127-03-9 and reverse transcriptase-inhibited HIV anticipates a composition comprising an inactivated retrovirus.

Claims 24-26, 28, and 29 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Levine et al. WO 93/15730 for reasons of record.

Applicant asserts that Levine et al. does not anticipate the instant invention because the sulfhydryl-reactive compound, 5,5'-dithiobis(2-nitrobenzoic acid) taught in the reference,

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inhibits the function of the viral protease and does not teach a composition comprising an inactivated retrovirus.

Applicant's assertions and a review of the reference have been considered, but are found unpersuasive because the compound of Levine et al., 5,5'-dithiobis(2-**nitro**benzoic acid), is a derivative of NO (emphasis added to the compound name). Therefore, the method of Levine et al. comprising the compound and the HIV with a disabled viral protease anticipates a composition comprising an inactivated retrovirus since the compound inhibits the virus replication.

Claims 24, 28, and 29 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Rice et al. (Nature. Feb., 1993, 361: 473-475) for reasons of record.

Applicant admits in the last full paragraph on page 11 that "...it was known in the art at the time of the invention that a C-nitroso compound having the formula: R-C-NO may be used for retroviral inactivation." This statement indicates that applicant and the art agree that R-C-NO inactivates retroviruses. Therefore, the teachings of Rice et al., which include inactivation of HIV-1 with a C-nitroso compound, anticipate the instant claims.

Applicant argues that Rice et al. does not anticipate the instant invention because the reference does not teach or suggest using C-nitroso compounds to dissociate zinc from CCHC zinc fingers. Dr. Rice reiterates this lack of teaching in the declaration as well as reasons for unpredictability for using unrelated compounds in the instant method.

Applicant's arguments have been considered, but are found unpersuasive because the mechanism of viral inactivation is not recited in the instant claims. Therefore, it is maintained

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that the derivative of nitric oxide, a C-nitroso compound and an inactivated HIV taught by Rice et al. clearly anticipate claims 24, 28, and 29.

Claims 24, 28, and 29 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Levine et al. (WO 92/15329) for reasons of record.

Applicant argues that the instant invention comprises an inactivated retrovirus that has been inactivated with certain compounds and that the instant claims differ from the teachings of Levine et al. because the reference teaches oxidatively inactivating HIV aspartyl protease with enzymatic and non-enzymatic metal-catalyzed oxidation systems.

Applicant's arguments and a review of the references have been considered, but are found unpersuasive. Levine et al. teaches a method for inactivating HIV with a copper compound that inactivates protease, see the abstract and the claims. The copper compound of the reference, i.e., "a copper ion delivery agent" anticipates the cupric ion complex of the instant claims. Therefore, the HIV inactivated by the copper ion delivery agent in the method of Levine et al. anticipates the instant composition claims.

### ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

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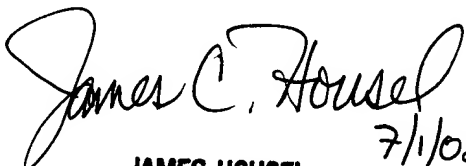
CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

  
Shanon Foley/SAF  
June 25, 2002

  
JAMES HOUSEL  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600  
7/1/02